Essential Needs and Current Gaps: Regulatory Support: FDA and Influenza Vaccines

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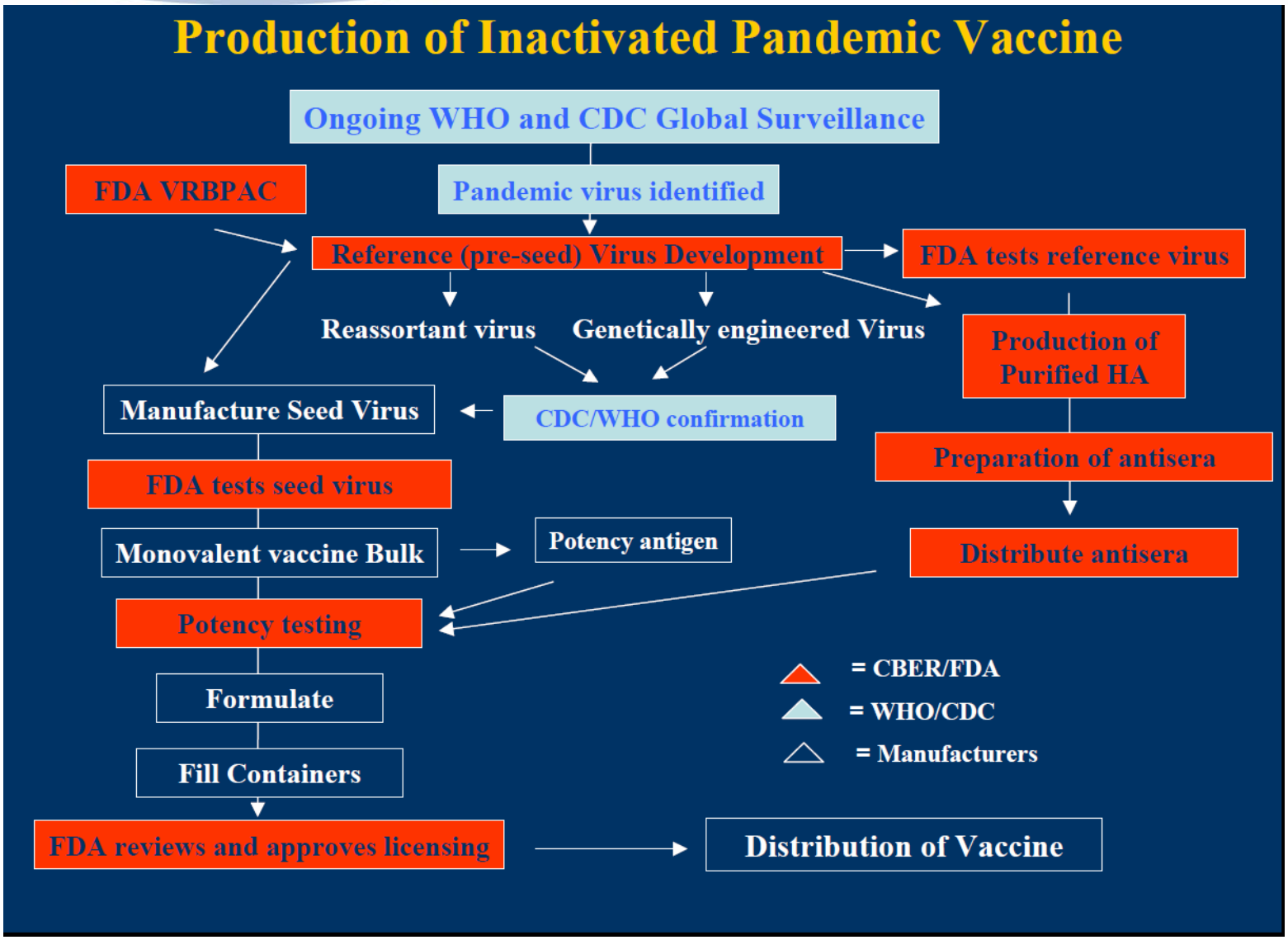
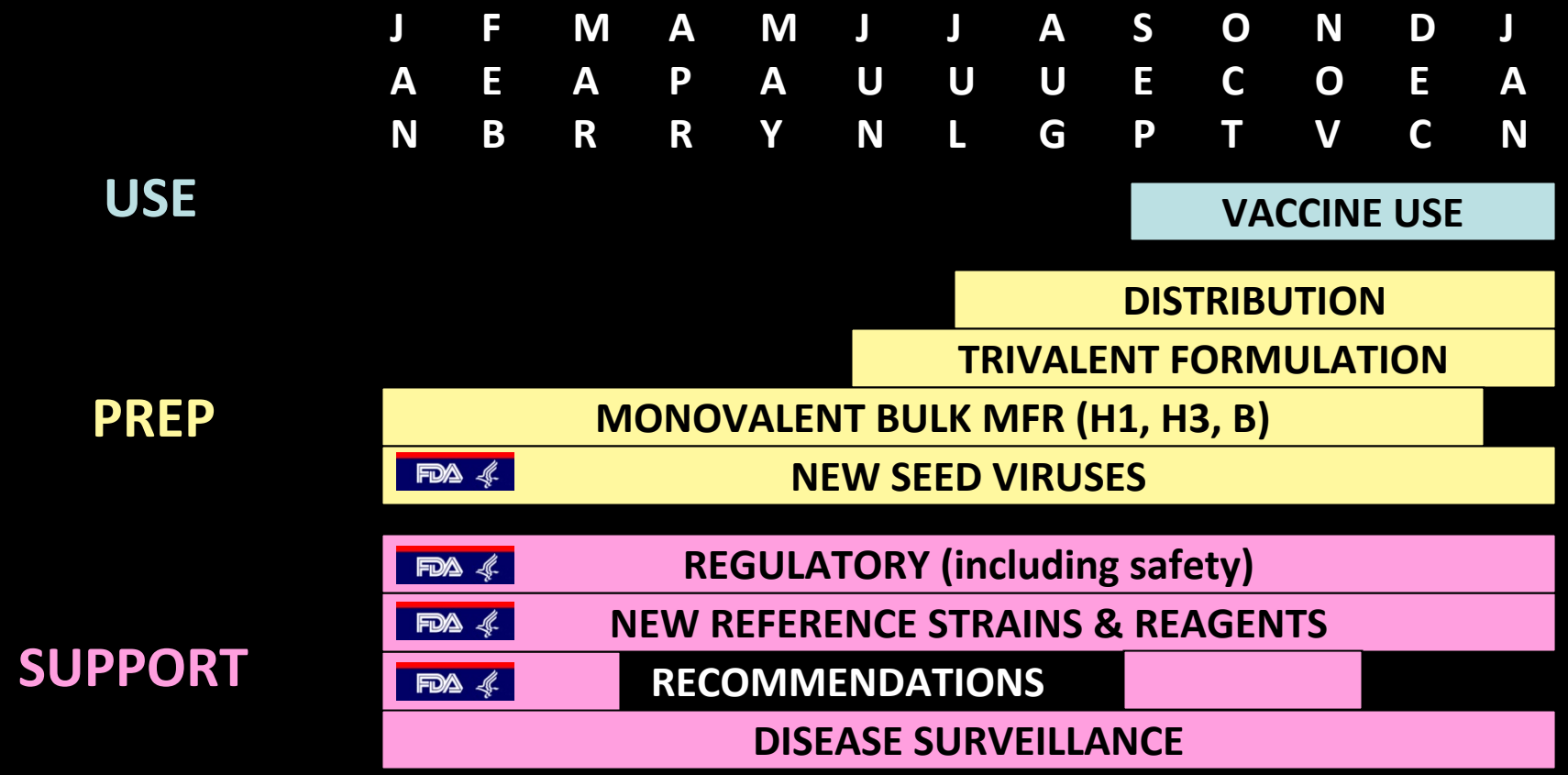
Vaccine regulation

- Initial licensure involves a thorough review of data submitted by the manufacturer, e.g.
  - Chemistry, manufacturing, and controls (includes preclinical studies, raw materials, manufacturing process (cGMP), product specifications (quality test results), stability, assays and their validation, product testing, etc.)
  - Clinical studies (including bioresearch monitoring)
  - Facilities review (includes inspections)
  - Advisory committee review
  - Labeling & indication
- After licensure, continued regulatory interactions, e.g.
  - Lot release and product testing
  - Manufacturing supplements
  - Inspections
  - Annual reports
  - Post-marketing surveillance
- Vaccine regulation is a major factor in public confidence, and therefore in utilization of vaccines



Regulatory infrastructure is also needed to assure that manufacturing is done according to license

Timeline for Seasonal Influenza Vaccine Production



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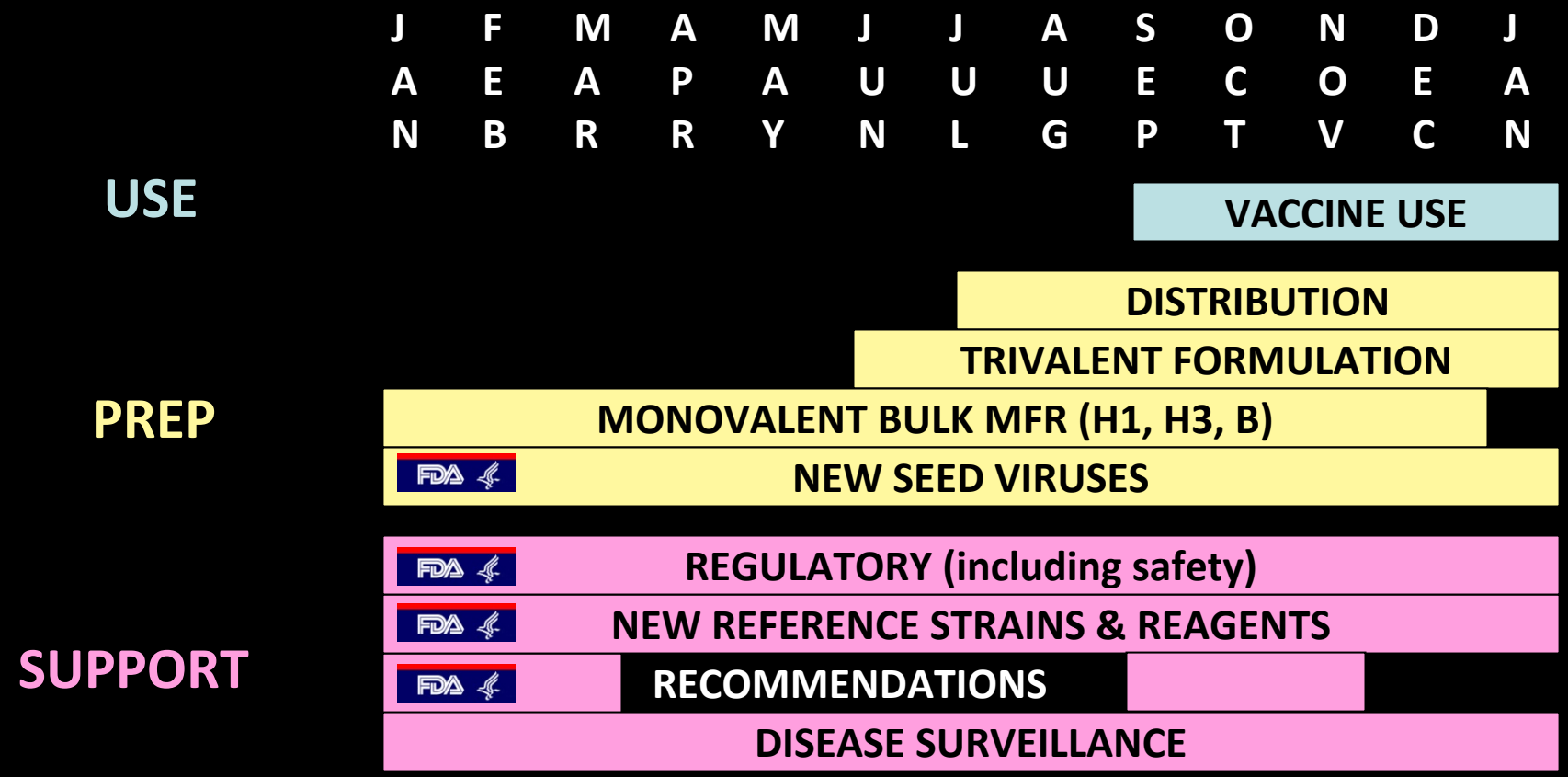

H1N1 Pandemic declared

- New ref strains, seeds, & reagents
- Regulatory pathways
- Clinical studies
- Enhanced vaccine safety studies

FDA H1N1 Pandemic Activities

- **Regulatory pathways for critical countermeasures**
  - Vaccines from established, licensed manufacturers licensed as strain change, based on previous experience over many years in many millions of vaccine recipients
    - Same egg based manufacturing process as licensed seasonal vaccines
    - Same in-process controls as licensed seasonal vaccines
    - Same lot release requirements as licensed seasonal vaccines
    - Same clinical data requirements as licensed seasonal influenza vaccines
    - US influenza vaccines do not contain adjuvants
  - FDA authorized the use of tests that can detect H1N1 influenza
  - FDA worked to assure the availability of antivirals that can be used to treat H1N1 influenza

FDA H1N1 Pandemic Activities

- **Clinical studies**
  - Clinical testing is not required for inactivated seasonal vaccines
    - Live-attenuated vaccine is tested in people for safety before it is approved
  - FDA worked with manufacturers, NIH to develop appropriate studies to gather dosing, scheduling, additional safety information for H1N1 vaccine

FDA H1N1 Pandemic Activities

- **Enhanced vaccine safety studies**
  - **Vaccine safety perspectives**
    - **People consider vaccine safety in the context of vaccine benefit**
    - **Public confidence in vaccination programs is always important, but is particularly critical when herd immunity is a goal**
    - **The public generally does not have more confidence in vaccine safety than it does in its regulatory process**
    - **Public mistrust of one vaccine may spill over onto other vaccines**
    - **With widespread use of new vaccine, there is an expectation of reports of adverse events after vaccination. It is important to be able to determine if they are truly vaccine associated.**

FDA H1N1 Pandemic Activities

- **Enhanced vaccine safety studies**
  - FDA worked with NVPO, CDC, CMS, IHS, DOD & others to improve our ability to assess any reports of adverse events after vaccination
  - FDA is working with international authorities so that data from other countries can also inform US decision-making
  - Data are subject to coordinated review by H1N1 Vaccine Safety Risk Assessment Working Group

H1N1 Influenza Vaccine Safety Monitoring Activities

System	Sponsor	# subjects
Vaccine Adverse Event Reporting System (VAERS)	CDC/FDA	passive
Vaccine Safety Data Link (VSD)	CDC	~9.5 million
Centers for Medicare & Medicaid Services Databases	CMS	~37 million
Post-Licensure Rapid Immunization Safety Monitoring (PRISM)	HHS, FDA & CDC	~39 million
Dept of Veterans Affairs Databases	VA	~11 million
Defense Medical Surveillance System (DMSS)	DoD	~2.6 million
Indian Health Service Resource and Patient Management Database	IHS	~1.4 million
Vaccines & Medications in Pregnancy Surveillance System (VAMPSS)	BARDA	~2400
Clinical Immunization Safety Assessment (CISA)	CDC	
Emerging Infections Program (EIP), (GBS case-finding)	CDC	
Real-Time Immunization Monitoring System (RTIMS)	CDC	

http://www.flu.gov/professional/federal/fed-plan-to-mon-h1n1-imm-safety.pdf

Summary of Key Regulatory Activities

- Vaccine licensure, inspections, other regulatory interactions with manufacturers
- Reference strains, seeds, and reagents
- Regulatory pathways for critical countermeasures
- Clinical studies
- Vaccine safety studies